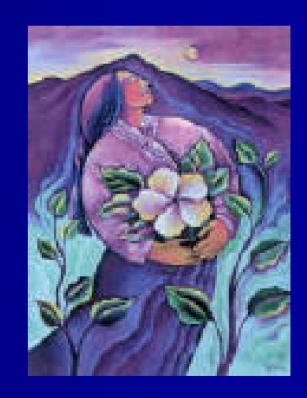
Integrative Approaches to Gestational Diabetes

Diane Downing
Integrative Family Medicine Fellow
University of Arizona
Program in Integrative Medicine
February 22, 2006



Objectives

Participants will:

 understand the usefulness and efficacy of 3 botanicals/supplements used in Diabetes Mellitus and its appropriateness in Gestational Diabetes

 be familiar with 2 integrative approaches to Gestational Diabetes

Gestational Diabetes

 Defined as a carbohydrate intolerance of variable severity with onset or first recognition during pregnancy



Prevalence-

- Diabetes most common medical complication of pregnancy
- Incidence of diabetes complicating pregnancy has increased about 40 percent between 1989 and 2002 (Martin and colleagues, 2003).
- In 2002, ~ 131,000 pregnancies complicated by diabetes, representing 3.3 percent of all live births (Martin and colleagues, 2003).
- More than 90 percent were gestational diabetes

Consequences

More than half of women with gestational diabetes will go on to develop overt diabetes in the ensuing 20 years

 Growing evidence for long range complications in their children that include obesity and diabetes (Feig and Palda, 2002)

Potential Fetal Complications



- Gestational Diabetes-Class A1
 - macrosomia
 - shoulder dystocia
 - brachial plexus injury
 - Neonatal hypoglycemia
 - fetal anomalies are NOT increased (Sheffield and colleagues, 2002)

- Overt Diabetes and Class A2 and above
 - spontaneous abortion
 - preterm delivery
 - stillbirth
 - congenital malformations
 - neonatal morbidity
 - complications as in gestational diabetes

Potential Maternal Complications



- Gestational
 - C-section
 - increased risk of CV complications
 - elevated lipids
 - HTN
 - metabolic syndrome

Overt

- 10 fold increase risk of maternal death (Cousins, 1987).
- ketoacidosis
- preeclampsia
- retinopathy
- neuropathy
- infections

Goals of therapy

- Fasting plasma glucose <95 mg/dL</p>
- 2 hour postprandial blood glucose < 120mg/dL





Mary's Story



Mary

- 26 y/o Hispanic G1P0
- 25 weeks gestation
- 1 hour glucose tolerance test 160 mg/dL
- 3 hour glucose tolerance test also abnormal
- Family Hx Mom with diabetes mellitus on insulin w/ h/o gestational diabetes when pregnant with Mary
- Eats a diet high in sat fat and carbohydrates

Current Care Strategies

- Diet –
- Exercise –
- Insulin- started when FBG persists >105 mg/dL
- Oral hypoglycemics not currently recommended by ACOG

Diet



- Nutrition counseling
- 30 kcal/kg/d based on pre-pregnant weight
- if obese caloric restriction

- Fresh fruits and vegetables
- Low glycemic index carbohydrates
- Whole grains
- High fiber oats
- Low saturated fat
- Low fat dairy
- Avoid refined sugar

Diet -

Oats –

- Pilot crossover study 8 Type II diabetic males
- High fiber oat bran concentrate bread product x
 12 weeks (34 gm/d fiber)
- vs. diet with 19 gm/d fiber
- after 24 weeks lower postprandial glucose and insulin levels
- lower total and LDL cholesterol and TGA
- (Pick, et al. 1996)

Diet -

Fiber –

- Small randomized crossover study of 13 Type II diabetic patients
- 6 weeks high fiber 50 gm/d (25 gm soluble + 25 gm insoluble
- vs. 6 weeks moderate fiber 24 gm/d (8 gm soluble + 16 gm insoluble
- Results decreased preprandial glucose levels by 13 mg/dL, decreased TC, VLDL, TGA (Chandalia, et al. 2000)

Diet -

- Cinnamon
 - 2003 study 60 Type II diabetics
 - Dose -1,3 or 6 gm/day cassia cinnamon x
 40 days
 - Results decreased FBG (18-29%), TGA (23-30%), TC (7-27%) LDL (12-26%)
 (Khan, et al. 2003)
 - -1 tsp. cinnamon =4.75 grams

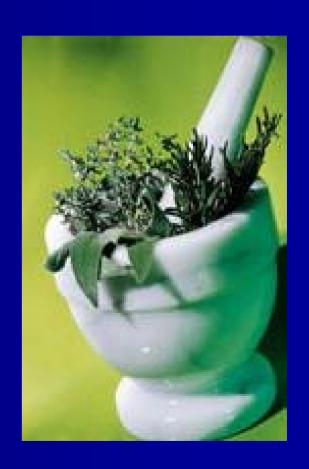
Exercise



- Physical activity during pregnancy reduces the risk of gestational diabetes (Dempsey and colleagues 2004)
- Resistance exercise helped avoid insulin therapy in overweight women with gestational diabetes (Brankston and associates 2004)

Potential Herbal Therapy in Diabetes Mellitus

- Gymnema
- Bitter melon
- Prickly Pear
- Fenugreek



Gymnema sylvestre

- Herb used in Ayurveda a traditional East Indian healing system
- Two non-randomized controlled clinical trials by same research group of Type I and Type II diabetics (Baskaran, et al. 1990. Shanmugasundaram, et al. 1990)
- Showed decreased fasting blood glucose,
 HgA1C and medication requirements
- Dose 400 mg GS4 water-soluble leaf extract
- Insufficient data for use in pregnancy



Bitter melon- *Momordica* charantia

- Vegetable eaten regularly in India, Asia, South America and Africa
- Small, preliminary study in Type I and II diabetics using injectable juice extracts showed acute reduction in BG at 30 min, 4 hr and 12 hr. (Baldwa et al. 1977)
- A case series looking at GTT after 50ml
 bitter melon fruit juice, and then after 8 11 weeks of fried melon bits
- Results 12% drop in GTT after juice, 6% after melon bits, 8% drop in HgA1c after bits (Leatherdale et al. 1981)



Bitter melon-

Type I and II diabetics have shown improved glucose tolerance and reduction in mean blood glucose levels (Yeh, et al. 2003)

Studies of poor quality and small size

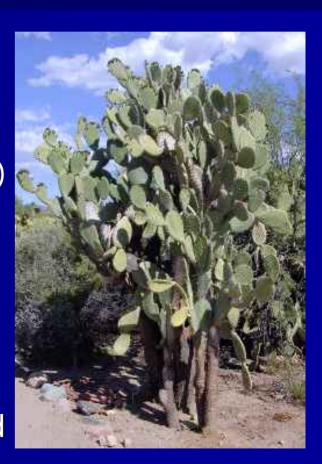
No studies in pregnancy

Bitter Melon - Safety

- Animal study showed a glycoprotein found in seeds to inhibit pregnancy in rats (Chan WY, Tam PP, Yeung HW. 1984.)
- Aqueous root extract abortifacient effects in mice (Aguwa CN, Mittal GC. 1983)
- Likely safe when eaten as a food
- Avoid extracts in pregnancy

Prickly Pear – "Nopales" - Opuntia streptacantha

- Commonly used by Mexican people for glucose control
- Two small studies in Type II diabetes (Frati, et al. 1988; 1990)
- Single dose 500 gm grilled or broiled stems
- Decreased fasting glucose and insulin levels
- No side effects reported
- Likely safe in pregnancy as a food



Nopales -

- May reduce blood sugar due to high fiber content
- 1 cup chopped pads = 60 calories = 5 grams fiber (20% of daily dose)
- Can be either grilled or added to vegetable dishes
- Available at many groceries

Fenugreek – *Trigonella foenum graecum*

- Legume cultivated in India,N. Africa and the Mediterranean
- Small study of Type I and II diabetics using defatted fenugreek seed powder, 100 gm/day in unleavened bread for 10 days (Sharma, et al. 1990)
- Results decreased fasting blood sugar, postprandial glucose, and urine glucose
- Side effects none



Fenugreek

- A study of 60 poorly controlled Type II diabetics
- Dose 25 grams of fenugreek seed powder divided into two doses at lunch and dinner
- After 24 weeks 47% achieved full glycemic control, 33% moderate control, 20% minimal control
- Significant improvement in fasting blood glucose and improved glucose tolerance (Sharma, et al. 1996)

Fenugreek - Safety

- Both water and alcoholic extracts exert a stimulating effect on isolated guinea pig uterus, especially during late pregnancy (Abdo MS, al Kafawi AA. 1969).
- May possess abortifacient effects, therefore, NOT recommended for use in doses higher than found in foods during pregnancy (Farnsworth et al. 1975).
- May be safe as a food
- Would NOT recommend an extract

Bottom Line for Herbs

In pregnancy –

Avoid extracts

Food sources likely safe

Supplements in diabetes mellitus

Chromium

Vanadium

Fish oil



Chromium picolinate



- Functions by regulating or potentiating insulin action
- Response time 10 days > 3 months
- Impaired glucose tolerance appears related to chromium deficiency
- In China, 833 Type II diabetics taking 500mcg/d were followed 10 months
- Results decreased fasting and postprandial glucose (Cheng, Zhu, Shi, 1999)
- Other studies with mixed results

Chromium picolinate

- Apparently one study in gestational diabetes
- Patients responded better to 8 mcg/kg of chromium picolinate than 4 mcg/kg (Jovanovic-Peterson, et al, 1996)
- No other studies in pregnancy
- Adequate Intake (AI) for pregnant women age 19-50 is only 30 mcg/day, above dose would be 500-600 mcg/d

Chromium picolinate - safety

- Some biochemical concern that reduction products may promote hydroxyl radicals and potential DNA damage
- However, animal studies show no carcinogenic or mutagenic effects in vivo
- Would NOT recommend to pregnant patients.

Vanadium



- 3 non-randomized, single-blind crossover studies (Cohen, et al. 1995; Halberstam, et al. 1996; Boden, et al. 1996.)
- Total of 21 Type II diabetics
- 100 mg/d vanadyl sulfate hydrate for 3-4 weeks
- Results decreased FBG, HgA1C, hepatic glucose production/output
- Side Effects- high rate of GI discomfort 18/21
- Insufficient evidence for safety in pregnancy for amounts > upper intake level of 1.8 mg

Fish Oil



- Cochrane Review showed no statistically significant effect on glycemic control (Farmer, et al. 2001)
- May have benefit on fetal/infant neural and retinal development when taken during last trimester of pregnancy (van Houwelingen, et al. 1995)
- May reduce risk of post partum depression
- May also be beneficial post-partum for breast-fed infants

Fish Oil

- Dose 1000 mg DHA/day
- Want a product free of methyl mercury
- Consumerlabs.com for good quality product
- Avoid fish with potentially high mercury level such as mackerel, swordfish, shark and tilefish

Yoga in Pregnancy



- Study of 166 pregnant patients trained in yoga, relaxation, meditation and breathing exercises
- Practiced 1 hour per day
- 164 controls received routine prenatal care
- Results indicated reduced rates of prematurity, maternal HTN, and improved birth weight in intervention group (Narendran, et al. 2005)

Yoga in DM II

- Study of 24 Type II diabetics (Singh, et al. 2004)
- Sequence of 13 asanas performed 30-40 min/day for 40 days under guidance.
- Significant decrease in fasting blood glucose levels of 50 mg/dL after yoga regimen.
- The postprandial blood glucose levels decreased 75 mg/dL
- Glycosylated hemoglobin showed a decrease from 1.2 %
- Blood pressure and pulse rate improvements also noted

Mind-Body Approaches

- Relaxation techniques such as:
 - progressive muscle relaxation
 - guided imagery
 - deep breathing exercises
- May provide some benefit with regard to lowering HgA1C (Surwit, et al. 2003))
- Will benefit the fetus by reducing maternal stress hormones (Bijlani, et al. 2005)



Postpartum

"Lifestyle behavioral changes, including weight control and exercise between pregnancies, likely would prevent recurrence of gestational diabetes as well as modify onset and severity of type 2 diabetes later in life" (Pan and associates, 1997).



Back to Mary

- Nutrition counseling and dietary changes
- May add prickly pear, beans, steel cut oats to diet for fiber, also add cinnamon
- Fish oil DHA 1000mg/day for Mom and baby
- Exercise Yoga
- Meditation Relaxation techniques
- Lifestyle changes postpartum

Thank you!



References

- Abdo MS, al Kafawi AA. Experimental studies on the effect of Trigonella foenum-graecum. Planta Med 1969;17(1):14-18.
- Aguwa CN, Mittal GC. Abortifacient effects of the roots of Momordica angustisepala. J Ethnopharmacol 1983;7(2):169-173.
- Baskaran K, Ahamath BK, Shanmugasundaram KR, Shanmugasundaram ERB: Antidiabetic effect of a leaf extract from *Gymnema sylvestre* in non-insulin dependent diabetes mellitus patients. *JEthnopharmacology* 30:295–305, 1990
- Baldwa VS, Bhandara CM, Pangaria A, et al. Clinical trials in patients with diabetes mellitus of an insulinlike compound obtained from plant source. Upsala J Med Sci 1977;82:39-41.
- Bijlani RL. Vempati RP. Yadav RK. Ray RB. Gupta V. Sharma R. Mehta N. Mahapatra SC. A brief but comprehensive lifestyle education program based on yoga reduces risk factors for cardiovascular disease and diabetes mellitus. Journal of Alternative & Complementary Medicine. 11(2):267-74, 2005 Apr. UI: 15865492
- Boden G, Chen X, Ruiz J, van Rossum GD, Turco S: Effects of vanadyl sulfate on carbohydrate and lipid metabolism in patients with non-insulin-dependent diabetes mellitus. *Metabolism* 45:1130–1135, 1996.

- Brankston GH, Mitchell BF, Ryan EA, et al: Resistance exercise decreases the need for insulin in overweight women with gestational diabetes mellitus. <u>Am J Obstet Gynecol</u> 190:188, 2004
- Chan WY, Tam PP, Yeung HW. The termination of early pregnancy in the mouse by beta-momorcharin. Contraception 1984;29(1):91-100
- Chandalia M, Garg A, Lutjohann D, et al. Beneficial effects of high dietary fiber intake in patients with type 2 diabetes mellitus. N Engl J Med 2000;342:1392-8.
- Cohen N, Halberstam M, Shlimovich P, Chang CJ, Shamoon H, Rossetti L: Oral vanadyl sulfate improves hepatic and peripheral insulin sensitivity in patients with non-insulin dependent diabetes mellitus. *J Clin Invest* 95:2501–250, 1995.
- Dempsey JC, Sorensen TK, Williams MA, et al: Prospective study of gestational diabetes mellitus in relation to maternal recreational physical activity before and during pregnancy. <u>Am J Epidemiol 159:663, 2004</u>
- Farmer A. Montori V. Dinneen S. Clar C. Fish oil in people with type 2 diabetes mellitus. [Review] [81 refs] Cochrane Database of Systematic Reviews. (3):CD003205, 2001. UI: 11687050

- Farnsworth NR, Bingel AS, Cordell GA, et al. Potential value of plants as sources of new antifertility agents I. J Pharm Sci 1975;64(4):535-598.
- Feig DS, Palda VA: Type 2 diabetes in pregnancy: A growing concern. <u>Lancet 359:1690, 2002</u>
- Frati AC, Gordillo BE, Altamirano P, Ariza CR, Cortes-Franco R, Chavez-Negrete A: Acute hypoglycemic effects of *Opuntia streptacantha Lemiare* in NIDDM (Letter). *Diabetes Care* 13:455–456, 1990
- Frati-Munari AC, Gordillo BE, Altamirano P, Ariza CR: Hypoglycemic effect of *Opuntia streptacantha Lemaire* in NIDDM. *Diabetes Care* 11:63–66, 1988
- Halberstam M, Cohen N, Shlimovich P, Rossetti L, Shamoon H: Oral vanadyl sulfate improves insulin sensitivity in NIDDM but not in obese nondiabetic subjects. *Diabetes* 45:659–666, 1996.
- Helland IB, Saugstad OD, Smith L, et al. Similar effects on infants of n-3 and n-6 fatty acids supplementation to pregnant and lactating women. Pediatrics 2001;108(5):E82.

- Jovanovic-Peterson L, Gutierry M, Peterson CM: Chromium supplementation for gestational diabetic women (GDM) improves glucose tolerance and decreases hyperinsulinemia. Diabetes 43:337a, 1996.
- Johnstone FD, Nasrat AA, Prescott RJ: The effect of established and **gestational diabetes** on pregnancy outcome. <u>Br J Obstet Gynaecol 97:1009, 1990</u>
- Khan A, Safdar M, Ali Khan M, et al. Cinnamon improves glucose and lipids of people with type 2 diabetes. <u>Diabetes Care 2003;26:3215-8.</u>
- Khalsa SB. Yoga as a therapeutic intervention: a bibliometric analysis of published research studies. [Review] [181 refs] Indian Journal of Physiology & Pharmacology. 48(3):269-85, 2004 Jul. UI: 15648399
- Leatherdale BA, Panesar RK, Singh G, et al. Improvement in glucose tolerance due to Momordica charantia (karela). Br Med J (Clin Res Ed) 1981;282(6279):1823-1824.
- Martin JA, Hamilton BE, Sutton PD, et al: Births: Final data for 2002. National Vital Statistics Reports, Vol 52, No. 10. Hyattsville, MD, National Center for Health Statistics, 2003
- Narendran S. Nagarathna R. Narendran V. Gunasheela S. Nagendra HR. Efficacy of yoga on pregnancy outcome. Journal of Alternative & Complementary Medicine. 11(2):237-44, 2005 Apr. UI: 15865489

- Pan XR, Li GW, Hu YH, et al: Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance. The Da Qing IGT and Diabetes Study. <u>Diabetes Care</u> 20:537, 1997
- Pick ME, Hawrysh ZJ, Gee MI, et al. Oat bran concentrate bread products improve long-term control of diabetes: a pilot study. <u>J Am Diet Assoc 1996;96:1254-61</u>.
- Shanmugasundaram ERB, Rajeswari G, Baskaran K, Kumar BRR, Shanmugasundaram KR, Ahmath BK: Use of *Gymnema sylvestre* leaf extract in the control of blood glucose in insulin-dependent diabetes mellitus. *J Ethnopharmacology* 30:281–294, 1990
- Sharma RD, Raghuram TC: Hypoglycemic effect of fenugreek seeds in non-insulin dependent diabetic subjects. *Nutr Res* 10:731–739, 1990
- Sharma RD, Raghuram TC, Rao NS: Effect of fenugreek seeds on blood glucose and serum lipids in type I diabetes. *Eur J Clin Nutr* 44:301–306, 1990

- Sharma RD, Sarkar A, Hazra DK, et al. Use of fenugreek seed powder in the management of non-insulin dependent diabetes mellitus. Nutr Res 1996;16:1331-1339.
- Sheffield JS, Butler-Koster EL, Casey BM, et al: Maternal diabetes mellitus and infant malformations.

 Obstet Gynecol 100:925, 2002
- Singh S. Malhotra V. Singh KP. Madhu SV. Tandon OP. Role of yoga in modifying certain cardiovascular functions in type 2 diabetic patients. Journal of the Association of Physicians of India. 52:203-6, 2004 Mar. UI: 15636309
- Surwit RS, van Tilburg MA, Zucker N, et al. Stress management improves long-term glycemic control in type 2 diabetes. Diabetes Care 2002;25:30-4.
- van Houwelingen AC, Sorensen JD, Hornstra G, et al. Essential fatty acid status in neonates after fishoil supplementation during late pregnancy. Br J Nutr 1995;74(5):723-731.
- Yeh GY. Eisenberg DM. Kaptchuk TJ. Phillips RS. Systematic review of herbs and dietary supplements for glycemic control in diabetes. [Review] [158 refs] Diabetes Care. 26(4):1277-94, 2003 Apr. UI: 12663610